

Exhibit I

Bladder Perforation During Tension-Free Vaginal Tape Procedures

Analysis of Learning Curve and Risk Factors

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OBJECTIVE: To estimate whether rates of bladder perforation decrease with increasing surgical experience.

METHODS: We performed a review of all patients undergoing a tension-free vaginal tape procedure performed by senior resident physicians under the guidance of a single surgeon. Physician experience was assessed by sequentially assigning case numbers to each procedure for each resident. For analysis of learning curve, cases were grouped in fives (ie, first five representing cases 1 to 5, second five cases 6 to 10).

RESULTS: Twenty-three residents performed 278 procedures. The median number of cases performed was 13 (range 3–22; mean number was 12.1 (sd = ± 5.6). The rate of perforation was 34.2% (95/278, 95% confidence interval 28.8–39.9%). Age and weight were significantly associated with perforation. The cystotomy group was, on average 4.5 years younger ($P = .007$) and 7.86 kg (17.3 lb) lighter ($P < .001$). Rate of injury in the first five series was 40.9%, 30.7% in second series of five, and 25.9% in the third series of five and was statistically significant (linear-by-linear association $\chi^2 = 4.286$, $df = 1$, $P = .038$). The relationship between the incidence of cystotomy and the cumulative number of cases performed was inversely correlated. As the number of cases a resident completed increased, there was a slight tendency for cystotomy to decrease ($P .033$). On cystoscopic examination, residents missed 35 of the 95 injuries (37%, 95% confidence interval 27.8–46.9%).

CONCLUSION: A learning curve exists for tension-free vaginal tape procedures. Many injuries are missed on

initial resident cystoscopic inspection, highlighting the need for comprehensive cystoscopic training during residency.

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LEVEL OF EVIDENCE: II-3

Cystotomy and voiding dysfunction have been noted to be the most common complications after tension-free vaginal tape.^{1–3} Factors predictive of urinary retention have been assessed; however, predictors of bladder injury have been much less studied.^{3,4} Surgeons have reported on learning curves with other new surgical techniques such as laparoscopy, but there is little information on transvaginal tape. Several authors have advised that the procedure “is safe when performed by experienced surgeons” and “the improvement in training programs, as is occurring with laparoscopy would be needed to minimize severe surgical complications.”⁵ A higher rate of bladder perforation during the first 7–10 procedures has been reported in the European literature.^{2,4,6} The prime objective of this study was to assess the learning curve among surgeons typically less experienced (ie, resident physicians) in transvaginal and retropubic incontinence procedures with the secondary goal of assessing general risk factors for bladder perforation.

MATERIALS AND METHODS

The study population consisted of 278 consecutive tension-free vaginal tape (Gynecare Inc., Sumerville, NJ) procedures (TVT), which were performed by senior resident physicians (in postgraduate years 3 and 4) under the guidance of a single surgeon (M.T.M.) from June 2000 to June 2004. All patients had genuine stress incontinence documented by multichannel urodynamic testing, which included a sitting cystometrogram, leak-point pressure at 150 mL and 200 mL, urethral pressure profiles, and voiding studies. Office cystoscopy was performed on those patients with mixed incontinence. The TVT was per-

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formed in the standard manner as described by Ulmsten et al⁷ with the following modifications: all procedures were performed under either general or regional anesthesia per patient preference. If multiple reconstructive procedures were performed, removal of the outer sheath was done on completion of all additional procedures. A curved scissor was placed between the tape and the urethra while the outer sheath was removed to ensure there was no overcorrection. All procedures were performed by a third- or fourth-year resident under direct supervision of the senior author. Passage of the tape typically occurred on the patient's right side initially if the surgeon was right handed and the left side if the surgeon's dominant hand was the left. Irrespective of handedness of the surgeon, the surgeon's right hand was used to direct the trocar on the patient's right and the left hand used to direct the trocar on the patient's left. If perforation was confirmed, the author performed the second passage. Those patients sustaining a bladder perforation had a 16F Foley catheter placed overnight. If there was no evidence of hematuria, the patient was instructed on how to remove the catheter themselves at home the next morning. In all cases, the Foley catheter was not removed until there was resolution of the hematuria. Patients who underwent additional reconstructive procedures had a suprapubic catheter placed, and voiding trials commenced when the urine was clear.

After obtaining approval through the St. Louis University institutional review board, hospital and office records were reviewed by the first author. Operative records of all patients having a transvaginal tape during the defined period were reviewed to identify the cases. General demographic data were extracted. Operating room time was extracted from anesthesia records for TVT-only group, which lists specific incision and end times. Physician experience was assessed by sequentially assigning case numbers to each TVT for each resident. For analysis of learning curve, cases were grouped in fives (ie, first five representing cases 1 to 5, second five cases 6 to 10, etc). As few residents performed more than 15 procedures, the 20 cases in the fourth grouping and 2 in the fifth grouping were excluded from the "learning curve" analysis to limit imprecise estimates resulting from small numbers.

Fisher exact test was used to assess the relationship between categorical variables and cystotomy, while the independent samples *t* test was used to assess relationships between cystotomy and continuous variables. The linear-by-linear association χ^2 statistic⁸ was used to assess the relationship between the

ordered "five cases" series and cystotomy. The directionality and strength of the relationship between the ordered "five cases" and cystotomy was confirmed using Kendall's τ -b.⁹ Finally, bladder perforation was analyzed with logistic regression controlling for patient age and weight. Statistical analysis was performed with SPSS 12.0 (SPSS Inc., Chicago, IL). A statistical power analysis, conducted with $\alpha = .05$, power = .80, and effect size estimates based on a review of the literature,³ resulted in a required sample size of 250 cases.

RESULTS

The mean age of the study patients was 57.8 years (range 30–85) and weight 80 kg (176 lb) with a range of 53–147 kg (117–325 lb). Of the 278 women, 123 (44%) had a TVT alone, and 155 (56%) had additional surgical procedures. Two hundred twenty-eight (82%) were performed under general anesthesia and 50 (18%) under spinal. Forty-six (16.5%) had a history of bladder surgery.

The overall rate of perforation was 34.2% (95/278, 95% confidence interval [CI] 28.8–39.9%). Thirty-five (12.6%, 95%CI 9.2–17.0%) were right sided, 42 (15.1%, 95% CI 11.4–19.8%) on the left, and 18 (6.5%, 95% CI 4.1–10.0%) bilateral. Of all bladder injuries, 36.8% (35) occurred on the right side, 44.2% (42) on the left side, and 18.9% (18) occurred on both sides. Three patients had prolonged hematuria from 5 to 7 days. Two of the three returned to the emergency room with acute abdominal pain secondary to catheter blockage from blood clots. One patient had two emergency room presentations.

Analysis of general risk factors showed no significant association among type of surgery, anesthesia, history of previous bladder surgery, and the risk of injury. Age and weight were significantly associated with perforation. Those patients who had a cystotomy tended to be, on average 4.5 years younger ($P = .007$) and 7.86 kg (17.3 lb) lighter ($P < .001$). For women only receiving a TVT (117 patients), operating room times were on average of 8.4 minutes longer ($P < .001$) for patients experiencing perforation (Table 1).

Twenty-three residents performed the 278 procedures. The median number of TVTs performed by each was 13 (range 3–22); the mean number performed was 12.1 (standard deviation ± 5.6). Of the cases, 110 (39.2%) represent the first five cases performed; 88 (31.7%) second five cases; 58 (20.9%) third five cases; 20 (7.2%) fourth five cases; 2 in fifth five group. As the numbers of cases in the fourth and fifth groups were small and therefore highly likely to yield unstable estimates of perforation, they were excluded



Table 1. Factors Associated with Perforation During a Tension-Free Vaginal Tape Procedure

| | No Perforation (N = 183) | Perforation (N = 95) | P |
|---|-----------------------------|-------------------------|---------|
| Age (y) | 59.32 | 54.83 | .007* |
| Weight (kg) | 83.0 | 74.7 | < .001* |
| Operating room time (min) for TVT alone (N=122) | 44.4 | 52.8 | < .001* |
| Type of anesthesia | | | .408 |
| General | 143 (63.8) | 81 (36.2) | |
| Regional | 35 (71.4) | 14 (28.6) | |
| History of previous bladder surgery | 33 (18.0) | 13 (13.7) | .398 |
| Type of surgery | | | .249 |
| TVT | 77 (63.1) | 45 (36.9) | |
| TVT plus additional procedures | 106 (67.9) | 50 (32.0) | |

TVT, tension-free vaginal tape procedure.

Data are presented as n (%) unless otherwise noted.

* Significant at or beyond the .05 level.

from further analysis. Of the remaining 256 operations, perforation occurred in 87 of 256 (34.0%, 95% CI 28.5–40.0%) with 32 (12.5%, 95% CI 9.0–17.1%) being right sided, 39 (15.2%, 95% CI 11.4–20.1%) on the left, and 16 (6.3%, 95% CI 3.9–9.9%) bilateral.

Learning curve analysis shows that more perforations occurred in the earlier cases (Table 2). This difference was statistically significant (linear-by-linear association $\chi^2 = 4.286$, $df = 1$, $P = .038$), and the relationship between the incidence of bladder perforations and the cumulative number of cases performed is in the expected direction (that is, inversely correlated; Kendall's $\tau_b = -.124$, $P .033$). Residents missed 35 of 95 injuries (37%, 95% CI 27.8–46.9%) on initial cystoscopic inspection.

The increasing experience of the senior supervising surgeon did not appear to lessen the risk of perforation, as the rate of perforation that occurred during the first group of five for those residents performing the procedure from June 2000 to December 2002 was 32% compared with 50% during January 2003 to June 2004. Residents missed 35 of 95 injuries (37%) on initial cystoscopic inspection. Two of the 23 residents (8.6%, 95% CI 2.4–26.8%) perform TVT procedures since graduation.

Multivariate analysis revealed that increasing age

and increasing weight were associated with a reduced likelihood of bladder perforation. However, increasing experience with the surgical procedure was not (Table 3).

DISCUSSION

As the TVT gains increasing acceptance as therapy for genuine stress incontinence and is increasingly performed by general gynecologists, there is a need to evaluate potential complications in surgeons traditionally less experienced with anti-incontinence procedures. Several experienced authors have recommended it be performed by surgeons with experience in transvaginal and retropubic procedures.^{1,3,6} In this study, we investigated general risk factors for the most common complication, that of bladder perforation, and specifically assessed the role of physician experience. Our data suggest that inexperienced surgeons have a higher perforation rate than more experienced surgeons with a perforation rate of 34% compared with the 4–15%, reported in the literature.^{1–3} In addition, it suggests that there is a definite learning curve to the TVTs. Previous reports have summarized the experience of senior gynecological surgeons⁴ or fellows under the direct guidance of a senior surgeon.¹ In this latter case, there was no mention as to the fellows' level of experience.¹

Table 2. The Learning Curve: Bladder Perforation by Number of Operations

| | 1st Five | 2nd Five | 3rd Five | Total |
|---------------------|-------------|-------------|-------------|------------|
| Bladder perforation | | | | |
| No | 65 (59.1) | 61 (69.3) | 43 (74.1) | 169 (66.0) |
| Yes | 45 (40.9) | 27 (30.7) | 15 (25.9) | 87 (34.0) |
| Total | 110 (100) | 88 (100) | 58 (100) | 256 (100) |

Linear-by-Linear Association $\chi^2 = 4.286$; $df = 1$; $P = .038$ Kendall's $\tau_b = -.124$; $P = .033$.**Table 3. Multivariate Analysis of Factors Associated with Bladder Perforation**

| Variable | Odds Ratio | 95% Confidence Interval | P |
|-----------------------|------------|----------------------------|--------|
| Case number performed | 0.936 | 0.873–1.004 | .063 |
| Age | 0.961 | 0.939–0.982 | < .001 |
| Weight | 0.985 | 0.977–0.993 | < .001 |



One European researcher assessed perforation rates during the learning phase of 6 senior surgeons.² They noted a higher perforation rate of 15% overall. The rate for the first 50 patients was 22% versus 8% for the second fifty patients. This corresponds to nearly two bladder injuries per surgeon for the first 10 cases. In our series, 72 injuries occurred in the first 10 cases, equating to just more than 3 per surgeon.

Bladder perforation is generally considered innocuous with most studies reporting no adverse outcomes. The most common consequence is prolonged bladder drainage. Lebre et al² noted no extensive bladder drainage beyond three days. Most other series have not reported on the needed length of catheterization after injury. In this series, three patients required prolonged catheterization for significant hematuria. Two returned to the emergency room for a blocked Foley catheter and required intermittent irrigation. In an effort to save discomfort, time, and money for a patient, one could argue that in a patient with gross hematuria after incidental cystotomy, gentle bladder irrigation could be taught and recommended if the catheter becomes blocked. None of these patients had a long-term complication from the hematuria or irrigation.

A recent report by Levin et al¹⁰ noted two cases of delayed diagnosis of intravesical tape made at 3 and 5 months postoperatively. These patients reported persistent urinary tract infections and severe irritative voiding symptoms. Both required repeated endoscopic excisions. This indicates that surgeons need to be skilled at cystoscopy.¹¹ Our study indicates that physicians less skilled in cystoscopy missed more than one third of the injuries. This potentially could increase the incidence of delayed tape perforation diagnoses. This author has noted that when the perforation is through and through, the bladder mucosa is often pinched together and the metal trocar is not easily visible. These perforations were the type generally missed by the residents. Therefore, surgeons need to be taught to maneuver the metal trocar in and out not just side to side to ensure that whole length of the trocar path can be visualized. This should help prevent the bladder walls from being compressed together.

One could argue that a perforation rate of 34%, much higher than the published rate and the fact that so few residents perform it after completion of residency, hardly justifies allowing a resident to perform the procedure on a patient. We would argue that this is the perforation rate that occurred while they were directly supervised by a senior surgeon on each case. If we do not supervise and teach them, a certain

number will graduate, take a one- or two-day course, and perform their initial cases without any supervision. By doing the procedure, the residents realize how easy it is for this complication to occur and for them to miss it. They have extra diligence when performing the cystoscopy and many decide not to perform the procedure in their own practices if they persistently perforate the bladder and/or miss the injury. It seems unlikely that they decide not to perform the procedure secondary to reimbursement issues as the procedure is well-compensated for a short procedure.

The side of perforation has not previously been assessed. It appeared that surgeons were more likely to perforate with their nondominate hand but this did not reach statistical significance. Once perforation occurs, it can be difficult to reassess the second passage either due to hematuria, which obscures the view and/or leakage of cystoscopy fluid, which makes distension more difficult. Knowing that perforations are more likely on the nondominant side, a case could be made for placing the tape on the side of the dominant hand initially so as to avoid potential difficulty with a second look should perforation occur.

Despite the fact that bladder perforation is the most common complication for the TVT, there is a paucity of information of other risk factors, which may be important in the counseling the patient preoperatively. Bodelsson et al⁶ discussed 26 cases of perforation in 177 operations and noted spinal anesthesia increased the risk when compared with local anesthesia. In this series of 95 injuries, type of anesthesia was not found to be a risk factor; however, spinal was compared with general anesthesia not local, and no additional risk factors were assessed in the former study, making direct comparison between the studies difficult. Previous bladder surgery did not appear to be a risk factor in this series; however, the numbers of patients who had previous surgery were low at 16.5%, which resulted in the study being underpowered to detect a difference with this variable. Abouassaly et al⁴ noted 3/14 patients with bladder perforation (21%) had a history of previous bladder surgery, which did not appear to be different from those without perforation (62/227, 27%).³

Age appeared to be a risk factor for perforation, with younger patients having higher rates. One possible explanation is that younger patients tend to have stronger endopelvic fascia, and therefore increased force is needed to perforate the tissue. Perforating the bladder should be a function of the aim of the trocar; however, the trocar has a wide curve, and therefore greater force could conceivably push it through a



wider arc as it suddenly breaks through the tissue and higher into the area of the bladder.

Increased body mass index does not appear to be a risk factor for bladder perforation with the TVT.^{12,13} Lovastis et al¹² noted in their series that all tape perforations occurred in nonobese patients; however, they all occurred in the first 65 of 159 procedures, so this may have represented a learning curve. An alternate explanation is that obese patients have an increased width of the pubic arch and therefore allow the surgeon to go more laterally compared with thinner patients. Unfortunately, we did not have documented heights on all patients, and therefore no body mass index was available. However, their study also noted that patients without perforation were significantly heavier.

In conclusion, bladder perforation is a common complication with TVTs. However, there do not appear to be any long-term complications if recognized intraoperatively. Resident physicians can be safely taught this procedure; however, the perforation rate in inexperienced hands is greater than with experienced surgeons. Perforations are easily missed on cystoscopy, and training in this procedure is critical.

REFERENCES

1. Karram MM, Segal JL, Vassallo BJ, Kleeman SD. Complications and untoward effects of the tension-free vaginal tape procedure. *Obstet Gynecol* 2003;101:929–32.
2. Lebreton T, Lugagne PM, Herve JM, Barre P, Orsoni JL, Yonneau L, et al. Evaluation of tension-free vaginal tape procedure: its safety and efficacy in the treatment of female stress urinary incontinence during the learning phase. *Eur Urol* 2001;40:543–7.
3. Groutz A, Gordon D, Wolman I, Jaffa AJ, David MP, Lessing JB. Tension-free vaginal tape for stress urinary incontinence: is there a learning curve? *Neurourol Urodynam* 2002;21:470–2.
4. Abouassaly R, Steinberg JR, Lemieux M, Marois C, Gilchrist LI, Bourque JL, et al. Complications of tension-free vaginal tape surgery: a multi-institutional review. *BJU Int* 2004;94:110–3.
5. Walters MD, Tulikangas PK, LaSala C, Muir TW. Vascular injury during tension-free vaginal tape procedure for stress urinary incontinence. *Obstet Gynecol* 2001;98:957–9.
6. Bodelsson G, Henriksson L, Osseir S, Stjernquist M. Short term complications of the tension free vaginal tape operation for stress urinary incontinence in women. *BJOG* 2002;109:566–9.
7. Ulmsten U, Falconer C, Johnson P, Jomaa M, Lanner L, Nilsson CG, et al. A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct* 1998;9:210–3.
8. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959;22:719–48.
9. Kendall MG. Rank Correlation Methods. Fourth ed. London: Griffin; 1970.
10. Levin I, Groutz A, Gold R, Pauzner D, Lessing JB, Gordon D. Surgical complications and medium-term outcome results of tension-free vaginal tape: a prospective study of 313 consecutive patients. *Neurourol Urodynam* 2004;23:7–9.
11. Wang AC. The techniques of trocar insertion and intraoperative urethrocystoscopy in tension-free vaginal taping: an experience of 600 cases. *Acta Obstet Gynecol Scand* 2004;83:293–8.
12. Lovastis D, Gupta C, Dean E, Lee F. Tension-free vaginal tape procedure is an ideal treatment for obese patients. *Am J Obstet Gynecol* 2003;189:1601–4.
13. Rafii A, Darai E, Haab F, Samain E, Levardon M, Deval B. Body mass index and outcome of tension-free vaginal tape. *Eur Urol* 2003;43:288–92.

